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September 11, 2004

PATENT APPLICATION
Attorney's Docket No.: 3033.1000-001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Darrell H. Carney

Application No.: 09/904,090 Group Art Unit: 1653

Filed: July 12, 2001 Examiner: Wax, R.A.

Confirmation No.: 1808

For: METHODS OF THERAPY WITH THROMBIN DERIVED PEPTIDES DERIVATIVES

CERTIFICATE OF MAILING OR TRANSMISSION

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, or is being facsimile transmitted to the United States Patent and Trademark Office on.

9-14-04 Sandra Brigham
Date Signature

SANDRA BRIGHAM
Typed or printed name of person signing certificate

DECLARATION OF DARRELL H. CARNEY, PH.D.
UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Darrell H. Carney, Ph.D., of 1125 Tallow Drive, Dickinson, Texas 77539, U.S.A., declare and state that:

1 I am one of the inventors of the subject matter described and claimed in U.S. Application No. 09/904,090 ('090), filed July 12, 2001.

2. I have been on the faculty at the University of Texas Medical Branch, 301 University Boulevard, Galveston, Texas 77555, U.S.A. since 1978, most recently as a Professor and Vice Chairman in the Department of Human Biological Chemistry and Genetics. I am also founder, President and Chief Executive Officer of Chrysalis BioTechnology Inc., 2200 Market Street, Suite 605, Galveston, Texas 77550, U.S.A. A copy of my curriculum vitae, which describes my educational and professional experience, is attached as Exhibit A.

I have published extensively in refereed publications, most of which have focused on the role of thrombin, thrombin peptides and thrombin receptors in cellular regulation. A list of publications authored or co-authored by me is included as part of my curriculum vitae.

3. I have found that ***endothelial cells have non-proteolytic high-affinity thrombin receptors (NPARs) and respond to compounds such as TP508 which activate the non-proteolytic thrombin cell surface receptor (NPAR)*** but do not have proteolytic activity to activate the proteolytically activated receptors (PAR1-PAR4).

The following is a description and discussion of the work performed by me or under my supervision and of the results which demonstrate that endothelial cells have non-proteolytic high-affinity thrombin receptors.

Thrombin Binding to Human Endothelial Cells

The specific binding of ^{125}I thrombin to cultures human microvascular (HMVE) and human aortic (HAE) endothelial cells (Clonetics, San Diego, CA) was carried out using established thrombin receptor binding assays as disclosed in U.S. Patent No. 5,352,664 and Carney, D.H. and Cunningham, D D., *Cell*, 15:1341-1349 (1978) Briefly, highly purified thrombin was iodinated and added to cultures of HMVE or HAE cells with or without unlabeled thrombin to correct for nonspecific binding. By incubating cells with different concentrations of labeled thrombin and measuring the amount of thrombin bound to cells and the amount of free thrombin in the medium, it is possible to estimate the number of receptors per cell and the affinity of thrombin for that binding site.

Scatchard analysis of labeled thrombin binding from several separate experiments indicate that human endothelial cells have two classes of high-affinity receptors on their cell surfaces. The binding results for HMVE cells are shown in Figures 1 and 2 (attached as Exhibits B and C, respectively). The binding results for HAE cells are shown in Figures 3 and 4 (attached as Exhibits D and E, respectively) The results indicate that HMVE cells have an average of $3.8 \pm 0.8 \times 10^3$ very high affinity binding sites per cell (Kd = 318 ± 88 pM; n = 3 ± SEM) and $1.1 \pm 0.3 \times 10^5$ high affinity sites (Kd = 16.9 ± 3.3 nM; n = 3 ± SEM). The results indicate that HAE cells have an average of $1.6 \pm 0.8 \times 10^4$ very high affinity binding sites per cell (Kd = 310 ± 124 pM; n = 2 ± SD) and $0.8 \pm 0.5 \times 10^5$ high affinity sites (Kd = 98 ± 70 nM); n = 3 ± SEM). This binding to endothelial cells is similar to that reported for high-affinity thrombin binding to fibroblasts (Carney, D.H. and Cunningham, D.D., *Cell*, 15.1341-1349 (1978)), and for which TP508 competes for binding (U.S. Patent No. 5,352,664 and Glenn, K.C. *et al.*, *J Peptide Research*, 1:65-73 (1989)) to initiate proliferative signals.

4. The subject application (the '090 Application) discloses results which demonstrate that ***compounds that activate NPAR, such as thrombin derivative peptides, stimulate endothelial cell proliferation and migration.*** In particular, the application discloses results which demonstrate that TP508 (SEQ ID NO: 3) has direct angiogenic effects on human microvascular endothelial (HMVE) cells causing increased proliferation and migration of the endothelial cells *in vitro* (Example 1). The application discloses results which demonstrate that HMVE cells respond to TP508 (SEQ ID NO: 3) resulting in increased proliferation and migration of the endothelial cells (Example 1).

5. The subject application also discloses results which demonstrate that ***thrombin derivative peptides have angiogenic activity which promotes cardiac tissue repair, stimulates revascularization of cardiac tissue and inhibits restenosis and vascular occlusion.***

In particular, the application discloses results which demonstrate that exposure of endothelial cells to TP508 has a protective effect to prevent death of cells caused by oxidative exposure, contributing to re-endothelialization and angiogenesis (Example 1) and that TP508 stimulates angiogenesis in a chorioallontoic membrane model (Example 2). The application also discloses results which demonstrate that TP508 can restore functionality to ischemic heart muscle (Example 3) and stimulate myocardial revascularization (Example 4). Additionally, the application discloses results which demonstrate that TP508 can significantly suppress restenosis and vascular occlusion (Example 5).

In summary, the application discloses results which demonstrate that the angiogenic thrombin derivative peptide of SEQ ID NO: 3 can promote cardiac tissue repair, stimulate revascularization of cardiac tissue and inhibit restenosis and vascular occlusion.

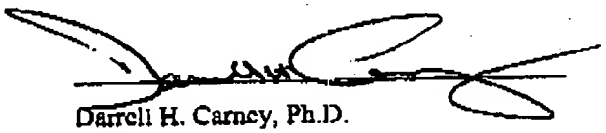
6. The results described herein in item 3 above provide evidence showing that NPARs are present on endothelial cells. The subject application provides evidence that TP508 has direct angiogenic effects on endothelial cell, causing increased endothelial cell proliferation and migration. The application also provides evidence demonstrating that the angiogenic thrombin derivative peptide TP508 can promote cardiac tissue repair, stimulate revascularization of cardiac tissue and inhibit restenosis and vascular occlusion. From the data, I conclude that TP508, a known NPAR agonist, acts on the NPAR present on endothelial cells to cause these effects.

Therefore, NPAR agonists other than TP508 would also cause endothelial cell migration and chemotaxis. I conclude that NPAR agonists other than TP508 would promote cardiac tissue repair, stimulate revascularization of cardiac tissue and inhibit restenosis and vascular occlusion.

7. Since thrombin derivative peptides of TP508 disclosed in U.S. Patent Numbers 5,352,664 and 5,500,412 have been shown to activate NPAR, these thrombin derivative peptides would also be expected to stimulate endothelial cell proliferation and migration, given the evidence that NPAR receptors are present on endothelial cells and

TP508 stimulates endothelial cell proliferation and migration. Thus, I conclude that these thrombin derivative peptides of TP508 would stimulate endothelial cell proliferation and migration. I also conclude that these thrombin derivative peptides of TP508 would promote cardiac tissue repair, stimulate revascularization of cardiac tissue and inhibit restenosis and vascular occlusion.

8. I declare that all statements made in this Declaration of my own knowledge are true and that all statements made on information and belief are believed to be true. Moreover, these statements are made with the knowledge that willful false statements and the like made by me are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.



Darrell H. Carney, Ph.D.

September 14, 2004

Date

Attachments

Exhibit A	Curriculum vitae, including list of publications
Exhibit B	Figure 1
Exhibit C	Figure 2
Exhibit D	Figure 3
Exhibit E	Figure 4

CURRICULUM VITAE

NAME: **Darrell Howard Carney** DATE: January 1, 2003

PRESENT POSITION AND ADDRESS:

Professor and Vice Chairman (September 2000)
Department of Human Biological Chemistry and Genetics
The University of Texas Medical Branch
Galveston, TX 77555-0645
(August, 1978)
Phone: (409) 772-3210
Fax: (409) 772-2348
Email: dcarney@utmb.edu

Chrysalis BioTechnology, Inc. (November 1995)
2200 Market, Suite 600
Galveston, TX 77550
Phone: (409) 750-9251
Fax: (409) 750-9253
Email: dcarney@chrysalisbio.com

BIOGRAPHICAL:

Date and Place of Birth:	April 15, 1948, Boise, Idaho
Citizenship:	USA
Social Security Number:	518-52-7622
Home Address:	1125 Tallow Drive Dickinson, Texas 77539
Phone:	(281) 534-3276
Fax:	(281) 337-4832

EDUCATION:

Institution	Date	Major	Degree
Northwestern University Evanston, Illinois	1966-68	Biology	
College of Idaho Caldwell, Idaho	1968-70	Biology	B.S.
University of Connecticut Storrs, Connecticut	1970-75	Developmental Biology	Ph.D.
University of California Irvine, California	1975-78	Cell Biology	Postdoctoral

EXHIBIT
A

PROFESSIONAL AND TEACHING EXPERIENCE:

1971-1972	Teaching Assistant in Developmental Biology and Human Anatomy, University of Connecticut
1972-1975	NIH Predoctoral Trainee Cell Biology Training Grant - GM 00317
1975-1978	NIH Postdoctoral Fellowship University of California, Irvine - CA 12306
1976-1978	Instructor in Medical Microbiology University of California, Irvine
1978-1982	Assistant Professor, Biochemistry Division, Department of Human Biological Chemistry and Genetics, The University of Texas Medical Branch, Galveston, TX (August 1978)
1978-Pres.	Biochemistry Program, Graduate School of Biomedical Sciences The University of Texas Medical Branch, Galveston, TX (August 1978)
1982-1992	Associate Professor, Division of Biochemistry The University of Texas Medical Branch, Galveston, TX (September 1982)
1986-1998.	Director of UTMB Peptide-DNA Synthesis Laboratory The University of Texas Medical Branch, Galveston, TX
1987-1988	Co-Director, UTMB Cancer Center Program; Hormone-Receptor Interactions in Cancer. The University of Texas Medical Branch, Galveston, TX
1992-Pres	Professor, Department of Human Biological Chemistry and Genetics, The University of Texas Medical Branch, Galveston, TX (September 1992)
1994-1995	Founder, Gal Tech Wound Therapies, DBA. 201 University Blvd. Suite 924, Galveston, TX (July, 1994)
1995-Pres	Founder and Scientific Director, Chrysalis BioTechnology, Inc. 2200 Market, Suite 600, Galveston, TX 77550 (November, 1995)
1997-Pres	President and CEO, Chrysalis BioTechnology, Inc. 2200 Market, Suite 600, Galveston, TX 77550 (July, 1997)
1998-Pres	Partner, Emprise Scientific, DBA of Emprise Partners, LTD. 1125 Tallow Drive, Dickinson, TX 77539 (July 1998)
2000-Pres	Vice Chairman, Department of Human Biological Chemistry & Genetics, UTMB. (September, 2000)

RESEARCH ACTIVITIES:

1968-1970 Undergraduate, College of Idaho, Biology Department
Independent Research, Funded by the Idaho Heart Association.

1970-1975 Graduate Research, University of Connecticut, Storrs, Connecticut. Departments of Animal Genetics and Genetics and Cell Biology, Norman W. Klein, Advisor. Biochemistry and Developmental Biology of brain development.

1975-1978 Postdoctoral Research, The University of California, Irvine, Department of Medical Microbiology,
Dennis D. Cunningham, Advisor Regulation of cell proliferation. Studies led to discovery and identification of thrombin receptors on the surface of fibroblasts and other cells.

1978-Pres. The University of Texas Medical Branch, Department of Human Biological Chemistry and Genetics. Role of thrombin receptors and thrombin-derived peptides in regulating cellular activities as they relate to inflammation, tissue repair, and cancer.

Based on our initial discovery of thrombin receptors on cells, our laboratories have studied the activation of these receptors and the subsequent signal cascades initiated by proteolytic and non-proteolytic thrombin interactions with cells. These studies have demonstrated that thrombin interacts with and activates a non-proteolytically activated thrombin receptor (NPAR) that is distinct from the proteolytically activated receptors (PAR1-4). Using synthetic peptides we identified the high-affinity binding domain of thrombin and discovered that the thrombin peptide TP508, representing this domain, activates NPAR and stimulates specific cellular activities that accelerate tissue repair. This peptide, also known as Chrysalin®, has been tested in Phase II safety and efficacy human clinical trials for accelerating the healing of chronic diabetic ulcers and orthopedic (distal radius) fractures. Based on positive results from these first trials, Phase II (diabetic ulcer) and Phase III (fresh fracture) trials will be initiated in 2002 by Chrysalis BioTechnology and its strategic partners Abbott Laboratories and OrthoLogic. In addition, human clinical trials to test the efficacy of thrombin peptides in spine fusion, cartilage repair, and myocardial revascularization are planned for initiation in 2002.

Because TP508 is proving to be an effective and potentially important molecule for orthobiologics, dermal tissue repair, prevention of vascular restenosis and revascularization of ischemic heart, basic science studies in our laboratory and in the laboratories of our collaborators are focusing on: (i) understanding the signal transduction pathways stimulated by activation of the non-proteolytically activated thrombin receptor (NPAR) in different tissues using array analysis and other techniques; (ii) cloning the NPAR receptor; (iii) and developing validated cell assays to screen peptide analogues and mimetics for activity.

RESEARCH SUPPORT

A. Previous Support

1978-79	Institutional Biomedical Research Support Grant DHEW 5-S07RR05427	$ 7,200
1978-79	Cancer Center Core Grant (CA 17701-04) "Thrombin Receptors in Normal and Transformed Cells"	8,750
1978-79	American Cancer Society Institutional Research Grant No. IN 112B	2,950
1979-80	UTMB Cancer Center - "Video Intensification of Cell Surface Molecules"	17,000
1979-82	DHEW 1R01-AM-25807, (01-03) "Role of Cell Surface in Regulating Cell Proliferation."	164,307
1982-87	DHHS 1 K04 CA00805, (01-05) Research Career Development Award	190,050
1982-87	DHHS 2R01 AM 25807, (04-08) "Role of Cell Surface in Regulating Cell Proliferation"	380,869
1983	Intramural Grant "Microinjection of Macromolecules into Single Living Cells."	21,500
1984-85	NSF PMC-8400954 "Acquisition of a Gas-Phase Protein Sequencer" (Co-P.I.)	65,000
1984-88	DHHS 1R01 GM 33505 "Studies of Cytoplasmic Microtubule Heterogeneity" (Co-investigator, 5% effort)	228,662
1985-86	Texas Neurofibromatosis Foundation, "Autocrine Stimulation of Neurofibromatosis by Growth Factors or Their Receptors."	9,091
1986-88	UTMB Administrative Support Grant, "Peptide and Oligonucleotide Synthesis Laboratory"	180,000
1987-88	DRR-BRS 1-S10RR03469, Principle Investigator "UTMB Peptide Synthesizer Facility"	95,500
1987-1997	UTMB Administrative Yearly Support Grant, "Peptide and Oligonucleotide Synthesis Laboratory"	30,000
1988-89	Monsanto Co./Searle, "Thrombin Peptides as Biological Response Modifiers"	40,000

1988-90	Texas Advanced Technology Program, "Thrombin and Synthetic Peptides in Wound Healing and Modulation of Biological Responses"	178,490
1989-92	Texas Advanced Technology Program, P. I., "Thrombin Peptides as Enhancers of Tissue and Bone Healing, and Inhibitors of Adhesions and Vascular Permeability"	200,000
1989-92	J. D. Searle. "Preclinical Evaluation of Thrombin Peptides as Enhancers of Wound Healing"	60,000
1987-93	DHHS 2R01 DK 25807 (09-15), "Role of Cell Surface in Regulation of Proliferation"	736,227
1992-94	American Diabetes Association, "Possible Acceleration of Diabetic Wound Healing with Thrombin and Synthetic Thrombin Receptor Activating Peptides"	79,941
1992-95	Johnson & Johnson Medical Inc., "Evaluation of Immobilized-TRAP-508 as a Wound Healing Device	43,976
1993-98	RO1-GM47572 "Role of Thrombin Peptides in Regulating Wound Healing." (P.I.) 5-years	591,950
1995	1 R43 AI38153-01 "Thrombin Peptide Effect on Cellular Antimicrobial Action" (Co Investigator, J. Stiernberg, Ph.D., P. I.)	100,000
1997-01	NIH 1R44-AI-38153 SBIR Phase II grant "Antimicrobial action of TRAP-508 (DHC, Co-Investigator, Janet Stiernberg, Ph.D., PI)	$750,000
1999-01	NIH-SBIR Phase I grant "Accelerated Fracture Repair Using Thrombin Peptides" (DHC-Scientific Director, Roger Crowther, PI)	$100,000
1997-01	NIH 1R44-DK 53580 SBIR Phase I/Phase II " Effect of Thrombin Peptides on Chronic Wounds" (DHC-Scientific Director, Laurie Sower, Ph.D., PI)	$850,000
1999-01	1 R 43 HL64508-01 NIH-SBIR Phase I Grant (A Norfleet, PI) "Inhibition of vascular restenosis by the TP508 peptide" (DHC-Scientific Director, Co-investigator)	$100,000
1999-01	1 R 43 AR46343-01 NIH-SBIR Phase I Grant (J. Stiernberg, PI) Cartilage repair induced by thrombin peptide TP508 (DHC-Scientific Director, Co-investigator)	$100,000

B. Current Support

D. H. Carney, Principal Investigator

1999-2003 CHR-001 "Molecular Mechanisms of Thrombin in Wound Healing, Inflammation, and Vascular Repair" Chrysalis BioTechnology, Inc. (P.I.) 800,000

D. H. Carney, Co-PI/Co-Investigator

1999-02 1R 44 AR 45508-02 NIH-SBIR Phase II Grant "Accelerated Bone Repair by a Synthetic Thrombin-Derived Peptide" (DHC-Scientific Director, Roger Crowther, PI) $750,000

2001-02 1R 43 HL69661-01 NIH-SBIR Phase I Grant "Revascularization of Ischemic Heart Tissue by TP508" (DHC- Co-Investigator, Chris Coleman, PI) $100,000

C. Pending Support

1 R 44 HL64508-02 NIH-SBIR Phase II Grant (C. Coleman, PI) "Inhibition of vascular restenosis by the TP508 peptide" (DHC-Scientific Director, Co-investigator) $750,000

1 R 44 NIH SBIR Phase I Grant (M. Keherly, PI) entitled "Enhanced Antimicrobial Activity by Synthetic Peptide NTP" (DHC, Co-investigator) $100,000

D. Patent Applications/Inventions

1986 "Thrombin Polypeptides :Composition and Methods for Use", **Darrell H. Carney** and Kevin C. Glenn, US. Patent Issued (5, 925,201) October 4, 1994. Issued, 10/04/94 Patent No 5,352,664.

1987 "Thrombin Peptides which Modulate Receptor Occupany and Mitogenic Stimulation", **Darrell H. Carney** and Kevin C. Glenn. European Patents 87 907 652.9-2110 (US87/02882), Issued.

1986 "Use of a Radiolabeled Monoclonal or Monovalent F(ab) Fragments of Monoclonal Antibodies for Quantitation of Cytoskeletal Antigens" (Invention Disclosure), WC Thompson, DH Carney and RL Ball.

1994 "Thrombin Peptides which Modulate Receptor Occupancy and Mitogenic Stimulation", Divisional Application for Use in Wound Healing. **Darrell H. Carney** and Kevin C. Glenn (#UTSG-043), Div. of (5, 925,201). US. Patent Issued Number 5, 500,412, March 19,1996.

1994 "Synthetic Peptide Neutrophil Cell Chemotactic Agents" **Darrell H. Carney** and Shyam Ramakrishnan (Disclosed to UTMB August, 1994), Patent Application 08/330,594 filed October 28,1994 (DC-006) by Chrysalis BioTechnology, Issued 10/30/01.

1995 "Thrombin Polypeptides: Composition and Methods for Use", **Darrell H. Carney** and Kevin C. Glenn, Divisional application for anti metastatic and inhibitory use of thrombin peptides to prevent unwanted proliferation or alteration of cellular function. (Pending).

2000 "Thrombin Derived Polypeptides: Compositions and Methods for Use. **Carney, D.H.** and Glenn, KC. Divisional Application #3033.1001-003 filed 8/02/00

2000 "Thrombin Derived Polypeptides: Compositions and Methods for Use. **Carney, D.H.** and Glenn, KC. Divisional Application #3033.1001-004 filed 8/02/00

2000 "Method of therapy with Thrombin Derived Peptides" **Carney, D.H.** Provisional Application for use of thrombin peptides in cardiovascular repair, inhibition of restenosis and myocardial revascularization. #3033.1000-000 Filed 07/12/00.

2000 "Stimulation of Bone Growth with thrombin peptide derivatives" **Carney, DH.**, Crowther, R., Simons, D., Redin, WR., Yang,J. Provisional application for use of thrombin peptides in repair of bone segmental gap filling, spinal fusion and areas where new bone growth are required. #3033.1002-000 Filed 7/19/00.

2000 "Stimulation of Cartilage Growth with agonists of the non-proteolytically activated thrombin receptor. **Carney, D.H.**, Crowther, R., Stiernberg, J., and Bergmann, J. Provisional application for use of thrombin peptides in cartilage and ligament repair, disc repair, etc. # 3033.1003-000 (60/219.800) filed 7/20/00.

2001 "Synthetic Peptide Neutrophil Cell Chemotactic Agents" **Darrell H. Carney** and Shyam Ramakrishnan (Continuation in part) filed June 2001

2001 "Method of therapy with Thrombin Derived Peptides" **Carney, D.H.** US, European PCT, Tiawan, and Thialand Applications for use of thrombin peptides in cardiovascular repair, inhibition of restenosis, and myocardial revascularization. #3033.1000-000. Filed on 07/12/01.

2001 "Stimulation of Bone Growth with thrombin peptide derivatives" **Carney, DH.**, Crowther, R., Simons, D., Redin, WR., Yang,J. US and European PCT application s for use of thrombin peptides in repair of bone segmental gap filling, spinal fusion and areas where new bone growth is required. #3033.1002-000. Filed on 7/19/01.

2001 "Stimulation of Cartilage Growth with agonists of the non-proteolytically activated thrombin receptor. **Carney, D.H.**, Crowther, R., Stiernberg, J., and Bergmann, J. US and European PCT for use of thrombin peptides in

cartilage and ligament repair, disc repair, etc. # 3033.1003-000 (60/219.800) filed 7/20/01.

2001 "Method for promoting healing of diabetic ulcers." Carney, D.H., Provisional US Application based on results of human diabetic ulcer trials. #3033.1008-000. Filed on 7/27/2001.

COMMITTEE RESPONSIBILITIES

A. National Committees/Editorial Advisory Boards/Manuscript Reviews, Etc.

1978-Pres.	Ad Hoc Reviewer of Manuscripts for: J. Biol. Chem., J. Cell. Biochem., J. Cell Biology, J. Cell. Physiol., J. Clin. Invest., FASEB Journal, Cancer Research, Lab. Investigation, Molecular Endocrinology, Nature, Federation Proceedings, Biochem. J., J. Pharmacological Res., Cell Motility and Cytoskelton, and National Science Foundation Grants.
1982	National Institute of Allergy and Infectious Diseases, Transplantation Biology and Immunology, Subcommittee (Program Project Study Section) (Ad Hoc Member)
1986	Neurological Sciences 1 Ad Hoc-2 Study Section
1986-90	Editorial Advisory Board, Molecular Endocrinology
1989	National Heart, Lung and Blood Institute, Program Project Site Visit (Albany, NY).
1989	Oklahoma Center for the Advancement of Science and Technology, Member, Study Section, (March, 19-21).
1989	Oklahoma Center for the Advancement of Science and Technology, Chair, Biomedicine/Biotechnology Study Section, (October 15-17).
1989-91	Consultant, J.D. Searle and Co., Wound Healing Agents.
1990	Oklahoma Center for the Advancement of Science and Technology, Chair of Chairs, Biomedicine/Biotechnology Study Session, (Feb. 18-20).
1991	Oklahoma Center for the Advancement of Science and Technology, Biomedicine - Biotechnology Study Session, (February)
1991-1997.	Consultant, Oklahoma Center for Advancement of Science and Technology
1992	NIH Clinical Sciences Study Section, subcommittee.
1994	NIH GM Special Study Section, Chronic Wound Healing.
1994-1995	Founder and Scientific Director, Gal Tech Wound Therapies.
1995-Pres.	Founder and Scientific Director, Chrysalis BioTechnology, Inc.
1998-99.	Wound Healing Society Program Committee

B. UTMB Committees

1. Graduate School of Biomedical Sciences Committees

1980-1988 Graduate Program Review Committee
1981 Vice-Chairman
1982-1988 Chairman
1988-1996 Scholarship Committee.
1992-1996 Chairman
1992-1996 Graduate Recruitment Committee

Advancement to Candidacy. Examination Committees

1979	Randall Kohl	Biochemistry
1980	John Scott Somerset	Genetics & Cell Biology
1980	Helena Hwu	Biochemistry
1980	Kathryn L. Crossin	Biochemistry
1981	Craig S. Woodard	Genetics & Cell Biology
1982	Gregory R. Alsip	Genetics & Cell Biology
1983	Rampyari Raja	Biochemistry
1983	Robin Cooper	Genetics & Cell Biology
1984	Gloria Frost	Biochemistry
1985	Hillary Heard	Microbiology
1985	Eve Johnson	Microbiology
1985	Jonathan Lloyd	Anatomy
1986	Eric Gordon	Biochemistry
1986	Gulzar Sandhu	Biochemistry
1986	Jonathan Lloyd	Anatomy
1987	Jerome Choate	Neuroscience
1989	Olapade James	Biochemistry
1990	Shyam Ramakrishnan	Biochemistry
1990	David Scott	Genetics & Cell Biology
1992	Dennis Kim	Biochemistry, Genetics & Cell Biology
1992	David Millinoff	Microbiology
1994	Laurie Sower	Microbiology
1996	David Hester	HBC & G
1997	Christie Bogolin	HBC & G

Masters Degree Supervisory Committees

1981-1982 M. Sheila Trumble, Pathology
1981-1983 Rebecca Ball, Microbiology
1988-1988 Nora Davis, Biochemistry, Supervisor
1989-1990 Fang Wang, Genetics & Cell Biology, Supervisor
1992-1992 Vanessa Paulley, Biochemistry, Genetics & Cell Biology, Supervisor

Ph.D. Supervisory Committees

1979-1980 John M. Nickerson, Genetics & Cell Biology
1980-1982 Kathryn L. Crossin, Biochemistry, Supervisory Professor,
1982-1984 Janet Stiernberg, Biochemistry, Research Supervisor
1982-1986 Robin Cooper, Cell Biology
1982-1986 Gregory R. Alsip, Genetics & Cell Biology
1984-1986 Rampyari Raja, Biochemistry

1982-1987 Hillary Heard, Microbiology
1983-1987 Rebecca Ball, Microbiology, Research Supervisor
1984-1987 Debra Morris, Preventive Medicine and Community Health, Research Supervisor
1985-1987 Sang-Uk Nham, Human Genetics & Cell Biology
1985-1991 Stephen Pearson, Biochemistry
1985-1988 Lawrence Smith, Microbiology
1986-1987 Gloria Herbosa, Biochemistry, Supervisory Professor
1986-1989 Eve Johnson, Microbiology
1986-1989 Eric Gordon, Biochemistry, Supervisory Professor
1987-1987 Johnathan Lloyd, Anatomy
1987-1990 Jerome Choate, Neuroscience
1988-1991 Alexandra Kemendy, Physiol & Biophys
1990-1995 David L. Scott, Human Genetics & Cell Biology, M.D./Ph.D. Program. S. Professor
1991-1994 Olapade James, Biochemistry, Genetics & Cell Biology, Supervisory Professor.
1992-1994 Shyam Ramakrishnan, Biochem Genetics & Cell Biology, Supervisory Professor.
1992-1994 Dennis Kim, Biochemistry, Genetics & Cell Biology, M.D./Ph.D. Program. Supervisory Professor.
1994-1995 Laurie Sower, Microbiology.
1994-1995 Juan Yu, Neurobiology.
1997-1999 BoJoy Yohanna, Microbiology
1997-1999 Kevin Bobbitt, Microbiology

2. School of Medicine Committees
   a. Past Committee Service

1981 Search Committee to select Chairman of Radiation - Cancer Therapy Department
1981 Search-Advisory Committee to select Director of Academic Computing and Biostatistics
1982-1983 Academic External Review Committee to review the Department of Anatomy
1983 Academic External Review Committee to review the Department of Microbiology
1984-1985 Faculty Advisory Committee, National Student Research Forum
1986 Search Committee to select Dean of the Graduate School and Research Vice-President
1987 External Review Panel to review the Department of Pharmacology
1987-1990 Elected Member of the Academic Planning Committee
1991 LCME Subcommittee for Self Study and Accreditation
1991-1993 Elected Member, Faculty Coordinating Council
1991-1993 Chair, Faculty Coordinating Council
1991-1993 Voting Member, Executive Committee of the Faculty of Medicine
1992-1993 Member Search Committee, Vice President for Public Relations and External Affairs
1984-1993 Intellectual Properties Committee (Patent Review Committee)
1986-1993 Chairman, Intellectual Properties Committee
1990-1993 Faculty Advisory Council -- Dean of Medicine
1989-1996 Advisory Committee for Continuing Medical Education
1995-1996 Nominating Committee

1996-1999. Technology Advisory Committee
1997-1999 Curriculum Committee Task Force - Dermal/Wound healing

b. Current Committee Responsibilities

3. Departmental Committees
a. Past Departmental Committee Service

1979 - 1985 Admission and Graduate Recruitment Committee - Biochemistry
1979 - 1990 Biochemistry Curriculum Committee
1982 - 1983 Departmental Travel Committee
1984 - 1990 Chairman, Biochemistry Credentials Committee
1986 - 1987 Departmental Recruitment Committee
1986 - 1988 Chairman's Advisory Committee
1989 - 1990 Departmental Recruitment Committee
1990 - 1992 HBC&G Graduate Program Credentials Committee
1991 - 1993 HBC&G Departmental Travel Committee
1991 - 1993 HBC&G Departmental Faculty Recruitment Committee
1993 - 1994 HBC&G Space Advisory Committee
1993 - 1995 Graduate Program Credentials Committee
1994 - 1997 Graduate Program Examination Committee
1995 - 1997 Chair, Graduate Program Exam. Committee
1995 - 1996 Chairman's Advisory Committee
1997-2000 Graduate Program Curriculum Committee

b. Current Departmental Committee Responsibilities

1998-Pres Compensation Advisory Committee
1999-Pres Chairman's Advisory Committee
1999-Pres Vice Chairman, Dept. of HBC&G
2000-Pres Department APT Committee

TEACHING RESPONSIBILITIES AT UTMB

A. Medical School

1987-1998 Medical Biochemistry, Cells and Genes 6501 - Lecture and SGSS on Cell Surface Receptors, Transport and Transmembrane Signals (five Lectures)

B. Graduate School

1979-1996 Biochemistry 6602 - Graduate Biochemistry Regulation and Control of Intermediary Metabolism (eight Lectures)

1979-1992 Biochemistry 6306 - Advanced Biochemistry Laboratory, Course Coordinator

1984-99 Fundamentals of Cell Biology 6407 - Receptor-Cytoskeletal Interaction, Transmembrane Signaling (4 lectures)

1991-97	HBC&G Special Topics, Growth Factors and Interleukins in Cellular Regulation. Course Co-coordinator (~20 hr of lecture, Course taught 1991, 92, 93, 95, 97).
1993- 1998	Cell Bio Program - Cell biology - Growth Factors and Cell Cycle Regulation (two lectures)
1993- 1996	Cell Bio Program- Biochemistry - "Energy and Intermediary Metabolism" and "Glycolysis" (two lectures)
1999 - present	BBSC Cell Biology 6204 Cell Cycle Regulation 4- lectures and/or one small group (alternating years).
2000-present	BBSC 6116 Inflammation Module, course co-director
2000-present	Cell Signaling Course, Co-director (~18 hours)

C. Current Graduate-Medical Students in Lab Training/Projects

none

D. Current Postdoctoral Fellows, Research Scientists, and Jr. Faculty

Janet Stiernberg, Ph.D.	Adjunct Assistant Professor in Human Biological Chemistry and Genetics, Successful PI on Wound Healing Project, NIH funded SBIR grants to study cellular antimicrobial activity of the thrombin peptide TP508 and its effect on chronic wound healing and cartilage repair.
Roger Crowther, Ph.D.	Adjuct Assistant Professor, Dr Crowther directs the Chrysalis BioTechnology Analytical Laboratory and oversees formulation and stability testing of TP508 products. PI on several Phase I/II SBIR NIH grants to study effects of TP508 in fresh fracture and other orthopedic applications.
Andrea Norfleet, Ph.D.	Preclinical Study Director. Dr. Norfleet is studying the mechanism of tissue repair stimulation by the TP508 peptide. Her initial projects involve identifying matrix and growth factor molecules that are stimulated early in tissue repair tissue by addition of TP508. In these studies she is using quantitative histology, immunocytochemistry, and *in situ* hybridization. She also obtained funding for a new SBIR project in vascular repair that demonstrated that TP508 may effectively reduce restenosis even in hypercholesterolemic rabbits.
Michael Kerheley, Ph.D.	Adjuct Assistant Professor, Group Director for BioDiscovery and Molecular Biology. Initial projects involve work on cloning the NPAR thrombin receptor and development of in vitro biological assays to test synthetic peptides for activity

related to tissue repair. Mike is also working on development of new technologies for tissue repair, modulation of infection and inflammation, and anti cancer applications

Mohammad Saeed Postdoctoral, BioDiscovery and Molecular Biology, focusing on receptor cloning projects. Recently, Mohammad has used the yeast-2 hybrid system to identify a family of proteins that bind to thrombin and thrombin peptides. He has also constructed expression vectors which can be tagged or expressed with GFP to study effects of TP508 expression in cells.

MEMBERSHIP IN SCIENTIFIC SOCIETIES:
American Society for Cell Biology
The Wound Healing Society
American Diabetes Association (professional)
European Academy of Science

HONORS:
Research Career Development Award, National Cancer Institute (1982-87).
Distinguished Alumni (Albertson College of Idaho, 1998).

ADDITIONAL INFORMATION

Invited Seminars, Symposia and Special Presentations

1978 "Proteases and Cell Proliferation." Panel Discussion ICN-UCLA Winter Symposium (March, Keystone, Colorado)

1980 "Relationship Between Cell Surface Receptors and Cytoplasmic Microtubules." International Symposium on Fundamental Mechanisms in Human Cancer Immunology, (Oct. 27, Galveston, TX).

1980 "Initiation of Cell Division by Thrombin-Receptor Interaction" UTMB Cancer Center Seminar Series (Sept. 16).

1981 "Surface Receptors and Cytoskeletal Interactions in Control of Normal and Neoplastic Cell Proliferation" UTMB Research Conference - Mini Symposium on Role of Cell Membranes in Control of Metabolism and Cell Behavior (June 23, Galveston, TX),

1981 "Preclustering of Thrombin Receptors and Their Interaction With Cytoplasmic Microtubules: Possible Role in Growth Regulation." Division of Endocrinology Research Seminar, The University of Texas Medical School at Houston (Houston, TX, Oct. 29).

1981 Chair, Platform Session on Receptor Mediated Endocytosis. American Society for Cell Biology (Nov. 10, Anaheim, California),

1982 "The Role of Microtubule Alterations in Initiation of DNA Synthesis" Federation of North Texas Area Universities 5th Annual Molecular Biology Symposium (May 21, Denton, Texas).

1982 "Role of Surface Receptors and Transmembrane Signaling in Initiation of Cell Proliferation" Department of Pharmacology Research Seminar, The University of Texas Medical Branch, Galveston, Texas, (Nov. 5)

1983 "Cell Surface, Receptors, Cytoskeleton and Receptor-Cytoskeletal Interactions." Two week lecture series - University of Puerto Rico, Rio Piedras, San Juan Puerto, Rico (Oct. 23-Nov. 1).

1984 "Mini symposia on Cellular Signal Transduction with Hormones, Mitogenesis and Oncogenes," American Society for Cell Biology (Nov. 13, Kansas City).

1984 "Microtubule Involvement in Initiation of Cell Proliferation" New York Academy of Sciences Conference on Dynamic Aspects of Microtubule Biology, (Dec. 3-6).

1985 "Thrombin Stimulated Phosphoinositide Metabolism Appears Necessary for Thrombin Mitogenesis," 69th Annual meeting of the Federation of American Societies for Experimental Biology, Anaheim, CA (April 21-26).

1985 "Double Lock Pathways Stimulated in Mitogenesis," Xth Congress of the International Society of Thrombosis and Haemostasis, San Diego, CA (July 15-18).

1985 "Role of Phosphoinositide Turnover in Thrombin Mitogenesis," 13th International Congress of Biochemistry -Amsterdam, The Netherlands (August 25-30).

1985 "Thrombin Receptor Occupancy Initiates Transient Increase in cAMP Levels in Mitogenically Responsive Hamster (NIL) Fibroblasts," New York Academy of Sciences, Conference on Bioregulatory Functions of Thrombin New York, NY (Feb. 5-7).

1985 Invited Seminar (International) "Thrombin receptors and transmembrane signals in regulation of cell proliferation" Centre de Biochimie, Seminar Program, Parc Valrose, Nice France (Sept. 1-4).

1986 International Workshop Organizer on Proteases and Biological Control. UCLA Symposium on Proteases, Park City, UT (Feb. 12).

1986 UTMB Representative, Special Conference on Academic-Industrial Interaction, Fisher Scientific Group, Hotel Del Coronado, San Diego, CA (July 10-13).

1986 "Modulation of Thrombin - Receptor Interaction in Cultured Neurofibroma and Neurosarcoma Cells," Texas Neurofibromatosis Foundation, Semi-annual meeting, Smithville, TX (Sept. 5).

1986 "Thrombin Peptide Interacts with High-Affinity Thrombin Receptors Initiating Part of the Proliferative Signal," Mini symposium on "Extracellular Proteases in Development and Neoplasia," at the 26th

Annual meeting of the American Society for Cell Biology, Washington, DC (Dec. 7-11).

1987 "Thrombin Stimulation of Proliferation: Role of Receptors, Cytoskeleton and Transmembrane Signals," Seminar-Department of Cell Biology and Anatomy, University of Alabama, Birmingham, AL (Feb. 18-20).

1988 "Thrombin Peptides Enhance Wound Closure and Increase Breaking Strength-Wound Healing Project Review." Monsanto Corporation Chesterfield, MO (March, 1988).

1988 "Mechanisms Involved in Thrombin Mitogenesis," Gordon Research Conference Speaker - Plymouth, NH (June 13-17).

1988 "Use of Synthetic Peptides as Probes for Receptor Ligand Interactions, Second Messenger Function and *in vivo* Modification of Biological Responses." Milligen Biosearch - National Frontiers in Molecular Biology Seminar Series.

1988 Invited Guest Speaker "Thrombin Receptors and Transmembrane Signals in Regulation of Cell Proliferation" Molecular Biology Seminar Series - University of Kansas, Lawrence KS (Feb. 3).

1989 "Thrombin and Synthetic Peptides in Wound Healing," Homecoming Address, The University of Texas Medical Branch, Galveston, TX (March 31).

1989 "Wound Healing Project Review - Research Alert." Monsanto Corporation, Chesterfield, MO (June 19-20).

1989 "Thrombin Peptides as Wound Healing Agents: Perspectives, Potential Efficacy, and Marketability," Monsanto Corporation - J.D. Searle and Company, Skokie, IL (August 30-31).

1990 "Thrombin and Thrombin Receptor Activating Peptides in Regulating Cell Proliferation *In Vitro and In Vivo*," University of Vermont Graduate Program Lecture Series in Cell and Molecular Biology, Burlington, VT (March 3-6).

1991 "Thrombin Peptides Promote Healing of Wounds in Steroid-Treated Rats." First International Meeting of the Wound Healing Society January 1991, Galveston, TX.

1991 "Synthetic Thrombin Peptides as Mediators of Cellular Processes *in vitro* and *in vivo*." Winter Neuropeptide Conference, Breckenridge CO, (February, 1991).

1991 "Postclotting Effects of Thrombin and Synthetic Thrombin Peptides: Potential Role in Wound Healing and Inflammation" Microbiology Seminar UTMB (May 1991).

1992 "Discovering Thrombin's Regulatory Diversity: Role of Thrombin and Thrombin Receptors in Cell Proliferation, Inflammatory Responses, and

Wound Healing." Faculty Research Colloquium: The University of Texas Medical Branch, (Jan. 27).

1992 "Research Update: Use of Synthetic Thrombin Peptides in Acceleration of Wound Healing." Johnson & Johnson Medical Inc., Dallas, TX (March 3-4).

1992 "Acceleration of Wound Healing and Thrombin Postclotting Cellular Activities *in vivo* using Synthetic Thrombin Receptor Activating Peptides" Somatix Therapy Corporation Seminar: Somatix Corp. Alameda CA. (April 24).

1992 "Role of Thrombin and Thrombin Receptors in Cell Proliferation, Inflammatory responses, and Wound Healing" Creative BioMolecules, Boston MA. (April 30).

1992 "Role of Thrombin and Synthetic Thrombin Receptor-Activating Peptides in Stimulation of Wound Healing, Inflammation, and Angiogenesis" Biogen Research Seminar. Boston, MA (August 6).

1992 "Stimulation of Wound Healing and Cellular Responses by Thrombin and Receptor Activating Thrombin Peptides" FASEB Conference on Structure and Function of Thrombin. Vermont (August 8-14).

1992 "Use of Synthetic Thrombin Peptides in Wound Healing." Research Update, Johnson & Johnson Medical Inc., Biopolymer Group, Stirling University, Stirling, U.K. (August 24).

1992 Delegate, 2nd European Tissue Repair Society Meeting, Malmo, Sweeden, (August 24-27). Johnson & Johnson Consultant

1993 Invited Research Seminar "Thrombin and Thrombin Peptides as Mediators of Inflammation and Tissue Repair" University of Houston, Biochemistry Department (March).

1993 State of the Art Lecture, "Role of Thrombin and Thrombin Peptides in Tissue Repair" International Congress of Thrombosis and Hemostasis, New York (July 3-12).

1993 "Efficacy of TRAP-508 in enhancing healing of incisional and open wounds in animal models" Spectrum Consumer Products, Houston TX (September 1993).

1994 "Effect of thrombin and thrombin peptides on corneal wound healing" Association for Research in vision and Ophthalmology, St. Petersburg Florida, (May 1994).

1994 Seminar, Thrombin Peptide Technology Update, Ventures Medical-Houston, TX (June 1994).

1994 Session Chair, "Thrombin and Cellular Systems" at the Fourth International Biennial Meeting on Blood Coagulation and Platelet Biology, "Thrombin functions and new Prospects in Antithrombotic therapy", Megeve, France, September 11-15, 1994.

1994 State of the Art Lecture, "Role of thrombin and thrombin peptides in initiation of inflammation and tissue repair" at the Fourth International Biennial Meeting on Blood Coagulation and Platelet Biology, Megeve, France, September 13, 1994.

1994 Invited International Seminar: "Role of thrombin and synthetic thrombin peptides in Inflammation and Wound Healing" University of Siena, Siena Italy, September 19, 1994

1995 Invited Seminar: "Effects of Thrombin and Synthetic Thrombin Peptides in Wound Healing" Cardiovascular Seminar Series, Sealy Center for Molecular Cardiology, UTMB, Galveston, TX.

1995 Discussant: FASEB Summer Conference on "Thrombin Structure and Function" Copper Mountain Colorado (August 1995).

1997 Seminar-Presentation: Thrombin peptides in wound healing. Biersdorf, AG, Hamburg, Germany. (January 10, 1997).

1997 Seminar-Presentations, "Thrombin Peptides in Wound Healing." Zurich Switzerland, Dr. Raphael Levi Feb. 13, 1997, and, Wuppertal, Germany, Bayer, AG. Feb. 14, 1997.

1997 Presentation, Bayer Biologics, New Haven, CT. "Thrombin and thrombin peptides in tissue repair" May 27, 1997.

1997 Presentation, US Surgical, New Haven CT., "Thrombin Peptide TP508 in soft and hard tissues: Potential therapeutic." May 28, 1997.

1997 Attendee: XVI Congress of the International Society on thrombosis and Haemostasis, Florence, Italy. June 4-11, 1997.

1997 Third FASEB Summer Conference on Thrombin, Saxon River Vermont. Meeting discussant - Presenter "Taking technology to market to support basic science research" August 9-13, 1997.

1997 Presentation: "Thrombin Peptide Use in Hard Tissue - Orthopedic Tissue Repair" OrthoLogic, Inc. Phoenix, AZ. October 13, 1997.

1997 Invited Seminar: Trinity University, SanAntonio, TX "Thrombin and Thrombin Peptides in Inflammation and Tissue Repair" Departments of Biology and Biochemistry October 20, 1997

1997 SBIR Workshop Presentation: "Opportunities to support basic science research using technology transfer and SBIR funding: Chrysalis BioTechnology, Inc. A Case Study" Universtiy of Texas Medical Branch health Science Center, Houston, TX. November 14, 1997.

1998 Keystone Winter Symposium, "Tissue Repair Mechanisms", Cooper Mountain, Colorado, January 10-14, 1998.

1998 Presentation to Drug Division, FDA "Use of Thrombin Peptide, TP508, in Surgical and Chronic Wound Healing, Pre-IND meeting. January, 20-21, 1998. Washington D.C.

1998 Invited Presentation. Arterial-Vascular Engineering (AVE), "Potential application of thrombin peptides for prevention of restenosis." January 29, 1998.

1998 Invited Presentation. Medtronic, Mineapolis Minn. "Potential application of thrombin peptides for prevention of restenosis." February 18, 1998.

1998 Invited Presentation. Medici Medical Technologies (The Edge Group), "Potential application of thrombin peptides for prevention of restenosis." February 20, 1998, Houston, TX.

1998 Invited Presentation. Guidant, San Francisco CA, "Potential application of thrombin peptides for prevention of restenosis." March 8-9, 1998.

1998 Seminar, UTMB Tissue Engineering Group, Pharmacology Conf. Rm., Synthetic peptides in Tissue Repair, Galveston, TX. March 10, 1998.

1998 OrthoLogic, Tempe, Arizona. "Use of Hyaluronic Acid as a vehicle for delivery of thrombin peptide, TP508." April 23, 1998.

1998 FDA presentation "Osteon" device for accelerated healing of fresh fracture. Presentation for device vs. drug determination for use of TP508 in orthopedic applications. April 29, 1998.

1998 Invited Seminar. "Use of TP508 for Interventional Cardiology" MIT, Cambridge Mass. Division of Cardiology. June 16, 1998.

1998 Wound Healing Society Annual Meeting, Oral Presentation. Thrombin peptide, TP508, stimulates wound healing through a non-proteolytic mechanism. Salt Lake City, Utah. June 20, 1998.

1998 OrthoLogic, Tempe, Arizona. Seminar, "Drug use of TP508 to accelerate fresh fracture healing." June 22, 1998.

1998 OrthoLogic, Tempe, Arizona. Meeting September 1, 1999

1998 Invited Cardiovascular Presentations, Guidant Corporation and AVE, September 9 and 10, 1998, California

1998 Invited Presentation, "Thrombin peptide TP508 use in soft and hard tissue repair." Trauma, Infection, and Repair Symposium, Galveston TX September 16,1998

1998 Invited Presentation, Washington DC "Effect of TP508 on neointima formation following angioplasty. AVE meeting with MIT collaborators. October 8,1998.

1998 Presentation and Discussions, UCSF. "Potential use of TP508 in spine fusion" November 12, 1998

1999 Invited Presentation. "New developments in Wound Healing with Chrysalin™ peptide TP508" 3M Corporation, Minneapolis, Minn. January 5, 1999.

1999 Invited Symposium Speaker Musculoskeletal Life Sciences Forum. "Tissue repair for the new millennium" Boston, Mass. January 27, 1999.

1999 Invited Presentation. "New developments in Wound Healing with Chrysalin™ peptide" Smith and Nephew, Tampa/St. Pettersburg, Florida. March 18, 1999.

1999 Invited Presentations (3). "New developments in Wound Healing with Chrysalin™ peptide" Baxter Hyland Immuno, Vienna Austria, Lohman Wound Care, Neuwied, Germany, and Smith Nephew, Hull, U.K. May 17-25, 1999.

1999 3rd Annual Biomaterials of the Future Conference, Medical Data International, SanFrancisco CA, "New advances in peptide technologies for repair of skin and bone" June 15, 1999.

1999 Symposium Speaker, Wound Healing Society, WOCN Joint Meeting and Educational Symposium, Therapeutic Possibilities for Problematic Wounds "Small Molecules for Wound Healing" Minneapolis Minn. June 20, 1999.

1999 Presentation to FDA, Washington DC, "Chrysalin™ for fracture healing in man" Pre-IND Meeting. July 15, 1999.

1999 Delegate, International Society for Thrombosis and Haemostasis Washington DC August 15-18,

1999 Attendee, Joint meeting of the European Tissue Repair Society and Wound Healing Society, Bordeaux France, August 24-28, 1999 .

1999 Presentation, "Thrombin peptide TP508 pre-clinical efficacy and Interim report on Diabetic Ulcer Trial DIAB001" Hollister, Chicago Illinois (September 2, 1999).

1999 Presentation, "Thrombin peptide TP508 pre-clinical efficacy and Interim report on Diabetic Ulcer Trial DIAB001" Healthpoint, San Antonio, TX (September 3, 1999)

1999 Presentation, "Thrombin peptide TP508 pre-clinical efficacy and Interim report on Diabetic Ulcer Trial DIAB001" Baxter Immuno Group Vienna Austria (September 8, 1999).

1999 Workshop on "Effects of thrombin and thrombin peptides on inflammatory cells and cytokines" Rome, IT (September 9-10, 1999).

1999 Civic Presentation "The Good Aspects of BioTechnology: Advances in wound care and bio engineering of tissues" Texas City Rotary Club

(November 2, 1999).

1999 Invited Seminar and Exploratory Discussion "Thrombin Peptides to promote repair of acute dermal, bone, and cardiovascular injuries: potential application to the Mars Mission" NASA, Houston, TX (November 9, 1999).

1999 Presentation, "Thrombin peptide TP508 pre-clinical efficacy and Interim report on Diabetic Ulcer Trial DIAB001" ConvaTec, Skillman, NJ (November 16-17).

2000 Presentation, "Thrombin peptide TP508 pre-clinical efficacy and Interim report on Diabetic Ulcer Trial DIAB001" Ross-Abbott, Coumbus Ohio (February 11, 2000).

2000 Invited Presentation "TP508 in Chronic Ulcers, Interim Data Diabetic Ulcer Trial DIAB001 and plans for international marketing" Abbott Laboratories (March 9, 2000).

2000 Co-Organizer and Speaker, 1st International Certosa de Pontignani Symposium: Thrombin and Thrombin Peptides in Inflammation and Tissue Repair. Siena, IT (May 13-16, 2000).

2000 Meeting and Discussions with companies:
Wound Healing Society Toronto, Canada (June 3-6,2000)

2000 Meeting and Discussions with companies: American Diabetes Association Meeting meet with clinical trial site coordinators San Antonio, TX (June 9-11,2000).

2000 Meeting and Discussions with companies: Direct Myocardial Revascularization, Washington DC (Separate meetings to set up collaborations to revascularize ischemic heart with Baylor and MicroMed Technologies), (June 21-23, 2000).

2000 Civic Presentation, "Chrysalis and Chrysalin ®, update on developing pharmeceutical companies in Texas" Representative Patricia Gray, Galveston, TX. (July 13,2000).

2000 Writing workshop (European Grant), Siena IT (August 16-22).

2000 Orthopedic TP508 Workshop, Sun Valley Idaho (August 30-September 2, 2000).

2000 Presentation, "Potential of TP508 in myocardial revascularization and inhibition of restenotic lesions" Abbott Laboratories Cardiovascular Development Group. (September 21, 2000).

2000 Participant, Tissue Repair Symposium, Virginia Commonwealth University, Richmond VA. (September 25-26, 2000).

2000 Invited Corporate Presentation (Delivered by D McWilliams) SouthWest BioVentures Conference, Moody Gardens (December 6, 2000).

2001 Thrombin Peptide Molecular Biology Symposium, Tremont House, Galveston TX (January 11-13, 2001).

2001 Presentation, "Effect of TP508 on porcine wounds and Othropedic update" (joint meeting with Chrysalis, Abbott, and OrthoLogic, Philadelphia, PA, March 12, 2001).

2001 Presentation, "TP508 interaction with NPAR, Background related to novelty of prior discoveries" U.S. Patent Office, Washington, DC. (June 5, 2001).

2001 Invited Speaker and Session Leader, 6th International Meeting on Angiogenesis: Basic Science and Clinical Developments. "Tissue repair stimulated by the angiogenic thrombin peptide, TP508" Crete, Greece (June 26-July 2nd, 2001).

2001 Invited Speaker, 3rd Annual Conference on Angiogenesis: Innovative Science and New Applications. "Thrombin Peptide TP508: An Angiogenic Factor that Accelerates both Dermal Wound Healing and Fracture Repair." Boston, MA (July 31, 2001).

2001 Delegate, European Tissue Repair Society Conference. Wales, UK (September 3-7, 2001).

2001 Investigators Meeting "Results of Phase II Trial Effect of TP508 on Diabetic Ulcers (Chrysalis DIAB001), Tremont House Hotel, Galveston, TX (September 8, 2001).

2001 Presentation, "Effects of TP508 on Distal Radius Fracture Phase I/II Trial (OrthoLogic)" FDA, Washington, DC (October 29, 2001).

2001 Invited Speaker & Roundtable Discussant, "Managing the Spinout Process: The Story of Chrysalis BioTechnology" SouthWest BioVenture Conference. Houston, TX (December 4-5, 2001).

2001 Four Poster Presentations, American Society for Cell Biology Annual Meeting, Washington DC (December 8-12, 2001).

BIBLIOGRAPHY

A. ARTICLES IN JOURNALS:

1. **Carney, D. H.** and Cunningham, D. D. Initiation of chick cell division by trypsin action at the cell surface. Nature 268: 602-666, 1977.

2. **Carney, D. H.**, Glenn, K. C. and Cunningham, D. D. Conditions which affect initiation of animal cell division by trypsin and thrombin. J. Cellular Physiol. 95:13-22, 1978.

3. Baker, J. B., Barsh, G. S., **Carney, D. H.** and Cunningham, D. D. Dexamethasone modulates the binding and action of epidermal growth factor in serum-free cell culture. Proc. Natl. Acad. Sci. USA 75:1882-1886, 1978.

4. **Carney, D. H.** and Cunningham, D. D. Cell surface action of thrombin is sufficient to initiate division of chick cells. Cell 14:811-823, 1978.

5. **Carney, D. H.** and Cunningham, D. D. Role of specific cell surface receptors in thrombin-stimulated cell division. Cell 15:1341-1349, 1978.

6. **Carney, D. H.** and Cunningham, D. D. Transmembrane action of thrombin initiates chick cell division. J. Supramol. Struct. 9:337-350, 1978.

7. **Carney, D. H.**, Glenn, K. C., Cunningham, D. D., Das, M., Fox, C. F. and Fenton, J. W., II. Photoaffinity labeling of a single receptor for alpha-thrombin on mouse embryo cells. J. Biol. Chem. 254:6244-6247, 1979.

8. Glenn, K. C., **Carney, D. H.**, Fenton, J. W., II and Cunningham, D. D. Thrombin active site regions required for fibroblast receptor binding and initiation of cell division. J. Biol. Chem. 255:6609-6616, 1980.

9. **Carney, D. H.** Visualization of thrombin receptors on mouse embryo fibroblasts using fluorescein-amine conjugated human-thrombin. J. Supramol. Struct. 13:467-478, 1980.

10. Crossin, K. L. and **Carney, D. H.** Evidence that microtubule depolymerization early in the cell cycle is sufficient to initiate DNA synthesis. Cell 23:61-71, 1981.

11. Crossin, K. L. and **Carney, D. H.** Microtubule stabilization by taxol inhibits initiation of DNA synthesis by thrombin and epidermal growth factor. Cell 27:341-350, 1981.

12. **Carney, D. H.** and Bergmann, J. S. ^{125}I-thrombin binds to clustered receptors on noncoated regions of mouse embryo cell surfaces. J. Cell Biol. 95:697-703, 1982.

13. Bergmann, J. S. and **Carney, D. H.** Receptor-bound thrombin is not internalized through coated pits in mouse embryo cells. J. Cell. Biochem. 20:805-817, 1982.

14. Stiernberg, J., LaBelle, E. F. and **Carney, D. H.** Demonstration of a late amiloride-sensitive event as a necessary step in initiation of DNA synthesis by thrombin. J. Cell. Physiol. 117:272-281, 1983.

15. **Carney, D. H.** Immunofluorescent visualization of specifically bound thrombin reveals cellular heterogeneity in number and density of thrombin receptors. J. Cell. Physiol. 117:297-303, 1983.

16. Thompson, W. C., Asai, D. J. and **Carney, D. H.** Heterogeneity among microtubules of the cytoplasmic microtubule complex detected by a monoclonal antibody to alpha tubulin. J. Cell. Biol. 98:1017-1025, 1984.

17. Stiernberg, J., **Carney, D. H.**, Fenton, J. W., II, and LaBelle, E. F. Initiation of DNA synthesis by human thrombin: Relationships between receptor binding, enzymic activity and stimulation of $^{86}Rb^{+}$ influx. J. Cell. Physiol. 120:289-295, 1984.

18. **Carney, D. H.**, Stiernberg, J. and Fenton, J. W., II. Initiation of proliferative events by human-thrombin requires both receptor binding and enzymic activity. J. Cell. Biochem. 26:181-195, 1984.

19. **Carney, D. H.**, Scott, D. L. and Gordon E. A. Phosphoinositides in mitogenesis: Neomycin inhibits thrombin-stimulated phosphoinositide turnover and initiation of cell proliferation. Cell 42:479-488, 1985.

20. Ball, R. L., **Carney, D. H.**, Albrecht, T. and Asai, D. J. and Thompson, W. C. A radiolabeled monoclonal antibody binding assay for cytoskeletal tubulin in cultured cells. J. Cell Biol. 103:1033-1041, 1986.

21. **Carney, D. H.**, Herbosa, G. J., Stiernberg, J., Bergmann, J. S., Gordon, E. A, Scott, D. and Fenton, J. W., II. Double signal hypothesis for thrombin initiation of cell proliferation. Seminars in Thrombosis Research 12:231-240, 1986.

22. Gordon, E. A and **Carney, D. H.** Thrombin receptor occupancy initiates cell proliferation in the presence of phorbol myristic acetate. Biochem. Biophys. Res. Comm. 141:650-656, 1986.

23. Frost, G. H., Thompson, W. C. and **Carney, D. H.** Monoclonal Antibody to the Thrombin Receptor Stimulates DNA Synthesis in Combination with Gamma-Thrombin or Phorbol Myristate Acetate. Journal of Cell Biology 105:2551-2558, 1988.

24. Glenn, K. C., Frost, G. J. Bergmann, J. S. and **Carney, D.H.** Synthetic peptides representing the thrombin-receptor binding domain bind to high-affinity thrombin receptors on fibroblasts and modulate thrombin mitogenesis. J. Peptide Research 1: 65-73 1989.

25. Ball, R.L., **Carney, D.H.** and Albrecht, T. Taxol inhibits stimulation of cell DNA synthesis by human cytomegalovirus. Experimental Cell Research 191:37-44. 1990.

26. Frost, G. H., Bergmann, J.S., and **Carney D.H.** Glycosylation of high-affinity thrombin receptors appears necessary for thrombin binding. Biochem. Biophys, Res. Comm. 180:349-355, 1991.

27. Hokanson, J.A., Hayward, P.G., **Carney, D.H.**, Phillips, L.G. and Robson, M.C. Mathematical models, life table methods, and the analysis of experimental wound healing data. Wounds 3: 213-220. 1991.

28. Belloni, P.N., **Carney, D.H.** and Nicolson, G.L. Isolation and partial characterization of murine and human endothelial cells from various organs: Differential responsiveness to thrombin and other growth factors. Microvascular Research 43 (1): 20-45, 1992.

29. Morris, D. L., Ward, J. B., Jr. Nechay, P., Whorton, E. B. Jr., Fenton, J. W., II and **Carney, D. H.** Highly purified human alpha-thrombin promotes morphological transformation of Balb / C 3T3 cells. Carcinogenesis 13 (1): 67-73: 1992.

30. **Carney, D.H.**, Mann, R., Redin, W.R., Pernia, S.D., Berry, D., Heggers, J.P., Hayward, P.G., Robson, M.C., Christie, J., Annable, C., Fenton, J.W., II and Glenn, K.C. Enhancement of incisional wound healing and neovascularization in normal rats by thrombin and synthetic thrombin receptor-activating peptides. J. Clin. Invest. 89:1469-1477, 1992.

31. Cromack, D.T., Porras-Reuys, B. H., Wee, S. S., Glenn, K. C., Pardee, J. A., **Carney. D. H.**, and Mustoe, T. A. Acceleration of soft tissue repair by a thrombin oligopeptide. J. Surgical Research 53: 117-122, 1992.

32. Ball, R.L., Albrecht, T., Thompson, W.C. & **Carney, D.H.** Thrombin, EGF, and PMA stimulate microtubule polymerization: A link to mitogenesis. Cytoskeleton and Cell Motility. 23: 265-278, 1992.

33. Naldini, A, **Carney, D. H.**, Borci, V. Klimpel, K.D., Asuncion, M., Soarer, L., & Klimpel, G.R. Thrombin enhances T cell responses and cytokine production. J. Cellular Immunol. 147: 367-377, 1993.

34. Pilcher, B.K., Kim, D.W., **Carney, D.H.** & Tomasek, J.J. (1994). Thrombin stimulates fibroblast-mediated collagen lattice contraction by its proteolytically activated receptor. Experimental Cell Res. 211, 368-373.

35. Kim, D., Wang, F, Ramakrishnan, S., Scott, D.L., Hensler, T.M., Thompson, W.C., and **Carney, D. H.** (1994). Fibroblasts defective in thrombin mitogenesis exhibit normal expression and activation of the proteolytically activated receptor for thrombin: Requirement for a second signaling pathway. J. Cell Pysiol. 160: 573-584.

36. Sower, L. E., Froelich, C.J., **Carney, D.H.**, Fenton, J.W.,II, and Klimpel, G.R. (1995) Thrombin induces IL6 production in fibroblasts and epithelial cells: Evidence for the invovement of the seven-transmembrane domain (STD) receptor for α-thrombin. J. Immunology. 155: 895-907.

37. Naldini, A. and **Carney, D.H.** (1996) Thrombin modulation of natural killer activity in human peripheral lymphocytes. J. of Cellular Immunology, 172:35-42.

38. Hallberg, C.K., Gill, K.S., Redin, W.R., Brown, JY., Brysk, M.M., **Carney, D.H.**, and Trocme, S.D. (1997). Enhancement of corneal epithelial wound healing by thrombin receptor activating peptide in the rat. Research Communications in Pharmacology and Toxicology 2: 129-136.

39. Naldini, A, Sower, L, Bocci, V., Meyer, R., and Carney, D.H. (1998). Differentiation-linked thrombin receptor upregulation and proliferative responses in human monocytes. J Cell Physiology 177: 76-84.

40. Sower, L.E., Payne, D.A., Meyers, R. and Carney, D.H. 1999. Thrombin peptide TP508 induces differential gene expression in fibroblasts through a non-proteolytic activation pathway. Exp. Cell Res. 247: 422-431.

41 Stiernberg,J Norfleet, A., J. Redin, W.R., Warner, W.S. Fritz, R, and Carney, D.H., 2000. Acceleration of full-thickness wound healing in normal rats by synthetic thrombin peptide, TP508. Wound Repair and Regeneration 8:3 204-215.

42 Norfleet, A., Wang, Y, Sower, L., Redin, W.R., Stiernberg, J., and Carney, DH. 2000. TP508 accelerates healing of full-thickness wounds in rat dermis with experimentally induced ischemia. Wound Repair and Regeneration 8: 517-529.

43 Naldini, A., Carney, D.H., Pucci, A., and Carraro, F. 2002 Human α-thrombin stimulates proliferation of interferon-γ differentiated, growth-arrested, U937 cells reversing differentiation-related downregulation of cyclin B and upregulation of p21. Submitted, J. Cell Physiol. 191:290-297.

44 Hedberg, E.L., Tang, A., Crowther, R.S., Carney, D. H. 2002 Controlled release of an osteogenic peptide from injectable biodegradable polymeric composites. Journal of Controlled release 84: 137-150.

B. BOOK CHAPTERS, REVIEWS, AND INVITED MANUSCRIPTS.

1. Carney, D. H. 1975. An analysis of the role of nutrient proteins in regulating the regional synthesis of specific proteins in early development of the chick embryo. Ph.D. Dissertation, University of Connecticut, Storrs CT.

2. Cunningham, D. D., Carney, D. H. and Glenn, K. C. Initiation of cell division by thrombin and trypsin. In Biology and Chemistry of Thrombin, Ed. by Lundblat, Mann, and Fenton, pp. 545-550, Ann Arbor Science, 1977.

3. Cunningham, D. D., Carney, D. H. and Glenn, K. C. A cell surface component involved in thrombin-stimulated cell division. In Hormones and Cell Culture-Cold Spring Harbor Conferences on Cell Proliferation, Ed. by Sato, G. H. and Ross, R., Vol. 6, pp. 199-215, Cold Spring Harbor Laboratory, 1979.

4. Carney, D. H. and Cunningham, D. D. Transmembrane action of thrombin initiates chick cell division In Transmembrane Signaling, Ed. by Fox, C. F., pp. 283-310, 1979.

5. Carney, D. H. and Crossin, K. L. Relationship between cell surface thrombin receptors and cytoplasmic microtubules: Potential involvement in regulation of normal and neoplastic cell proliferation. In Fundamental Mechanisms in Human Cancer Immunology, Ed. Saunders, J. P., Daniels, J. C., Serrou, B., Rosenfeld, C. and Denney, C. B., Chapter 4, Elsevier North Holland, N.Y., 1981.

6. Hillman, G. R., Johnston, D., Kwan, S.-W., **Carney, D. H.** and Childs, C. Histochemical applications of image analysis techniques. In Proceedings of the International Symposium on Medical Imaging and Image Interpretation, published by the Institute of Engineering and Electronic Engineers, 1982.

7. Cunningham, D. D., **Carney, D. H.**, Baker, J. B., Low, D. A., and Glenn, K. C. Role of cell surface components and receptors in thrombin-stimulated cell division. In Proteins in Biology and Medicine, Ed. by Bradshaw, R. A., Hill, R. L., Tang, J., Chih-Chuan, L., Tien-Chin, T. and Chen-Iu, T., pp. 43-59, 1982.

8. Albrecht, T., Li, J. L., Speelman, D., Ball, R., Nokta, M., Fons, M., Lee, C. H., Steinsland, O., Thompson, W. C. and **Carney, D. H.** Cellular responses to human cytomegalovirus infection. In CMV Pathogenesis and Prevention of Human Infection, Alan R. Liss, Inc., Ed. by Plotkin, S. A., Michelson, S., Pagano, J. S. and F. Rapp, Birth Defects: Original Article Series, Vol. 20, pp. 21-34, 1984.

9. **Carney, D. H.**, Crossin, K. L., Ball, R. L., Fuller, G. M., Albrecht, T. and Thompson, W. C. Changes in the extent of microtubule assembly can regulate initiation of DNA synthesis. Ann. of the New York Academy of Sciences 466:919-932, 1986.

10. **Carney, D. H.**, Thompson, W. C. Role of cytoplasmic microtubules in regulation of cell proliferation. In Prog. of Neuropathology 6:91-117, 1986, (H. M. Zimmerman, Ed.), Raven Press, New York, 1986.

11. Gordon, E. A and **Carney, D. H.** Thrombin receptor occupancy initiates a transient increase in cAMP in levels in mitogenically responsive hamster (NIL) fibroblasts. Ann. of the New York Acad. of Sci. 485:249-263, 1986.

12. **Carney, D. H.** Characterization of thrombin receptors and their role in initiation of cell proliferation. In "Cell Proliferation: Recent Advances," 141:265-296. (A. L. Boynton and H. L. Leffert, Eds.) Academic Press, Orlando FL. 1987.

13. **Carney, D. H.** Perspectives on the cellular and biochemical effects of thrombin interaction with surface receptors and substrate molecules. In Proteases in Biological Control and Biotechnology, Vol 57: 277-282, Alan R. Liss, Inc., 1987.

14. Pernia, S. D., Berry, D. L., Redin, W. R. and **Carney, D. H.** A synthetic peptide representing the thrombin receptor-binding domain enhances wound closure *in vivo*. In Southern Association for Agricultural Scientists, Vol 3: 8-12, 1990.

15. **Carney, D. H.**, Reddin, W. R., and McCroskey, L. M. Role of High-Affinity Thrombin Receptors in Postclotting Cellular Effects of Thrombin. Seminars in Thrombosis and Hemostasis. 18: 91-103, 1992.

16. **Carney, D.H.** Postclotting cellular effects of thrombin and thrombin receptor activating peptides in Thrombin Structure and Function, (ed. L. Berliner) Plenum Publishing Co., p351-387, 1992.
Stiernberg, J., Redin, W.R., Warner, W.S. and **Carney, D.H.** Role of thrombin and thrombin receptor-activating peptide (TRAP-508) in initiation of tissue repair. Thrombosis and Haemostasis. 70: 158-162, 1993.

17. Simmons, D. J., Yang, J., Yang, S., Bi, L.X., Buford, W. L., Turner, R. T., Crowther, R., and **Carney, D. H.** Acceleration of rat femoral fracture healing by a synthetic thrombin peptide. Calcium Metabolism: Comparative Endocrinology. Proc. Satellite Meeting, SanFrancisco CA, Nov. 30, 1998, Ed. C Dacke, J Danks, G Flik, & C Gay BioScientifica Ltd., Bradley Stoke, Bristol, UK. 1999.

18. Ryaby, J.T., Campbell, M.B., **Carney, D. H.**, Crowther, R.S., Yang, J., Simmons, D.J., Zoltan, J.D., and Magee, F.P., Acceleration of fresh fracture healing with an injectable thrombin peptide in a rat model., Proceedings of the American Academy of Orthopaedic Surgeons. Paper No 267, 2000

19. **Carney, D.H.** and Anderson, D.W. Angiogenesis to repair the heart. Biotech (January 2001) p 30-34.

20. Norfleet, A. M., Bergmann, M.S., and **Carney, D.H.** Thrombin peptide, TP508, stimulates angiogenic reponses in animal models of dermal wound healing, in chick chorioallantoic membranes, and in cultured human endothelial cells. J General Pharmacology: 35:249-255

21. Naldini, A., **Carney, D.H.**, Pucci, A., Pasquali, A., and Carraro, F. Thrombin regulates the expression of pro-angiogenic cytokines via proteolytic activation of PAR1. J. General Pharmacology.

C. ABSTRACTS

1. **Carney, D. H.** and Klein, N. W. The effect of protein starvation on the patterns of protein synthesis in the cultured chick embryo. Teratology 7:A-13, 1973.

2. **Carney, D. H.** and Klein, N. W. Selective effects of protein starvation on the synthesis of microtubule protein in the brains of early chick embryos. J. Cell Biol. 63:51a, 1974.

3. **Carney, D. H.** and Cunningham, D. D. Determination of polypeptide action at the cell surface. J. Cell Biol. 75:57a, 1977.

4. **Carney, D. H.** and Cunningham, D. D. Initiation of cell division by thrombin action at the cell surface. J. Supramol. Struct., Supplement 2, 134, 1978.

5. Baker, J. B., Barsh, G. S., **Carney, D. H.** and Cunningham, D. D. Dexamethasone modulates the binding and action of growth factors. J. Supramol. Struct., Supplement 2, 132, 1978.

6. **Carney, D. H.** and Cunningham, D. D. Demonstration of a surface receptor for thrombin on mouse embryo fibroblasts: Involvement in initiation of cell division. J. Cell Biol. 79:44a, 1978.

7. **Carney, D. H.**, Glenn, K. C., Cunningham, D. D., Das, M. and Fox, C. F. Photoaffinity labeling of the thrombin receptor on mouse embryo fibroblasts. J. Supramol. Struct. 9, Supplement 3:565, 1979.

8. Cunningham, D. D., **Carney, D. H.** and Glenn, K. C. Role of the cell surface in thrombin-stimulated cell division. J. Supramol. Struct. 9, Supplement 3:433, 1979.

9. **Carney, D. H.** Visualization of thrombin receptors using an FITC-amine labeled thrombin. J. Supramol. Struct., Supplement 4:170, 1980.

10. Glenn, K. C., **Carney, D. H.** and Cunningham, D. D. Binding and mitogenic potential of active-site modified forms of -thrombin to cells from various animal species. J. Supramol. Struct., Supplement 4:174, 1980.

11. Crossin, K. L. and **Carney, D. H.** Role of microtubule depolymerization in mitogenesis. J. Cell Biol. 87:252a, 1980.

12. Crossin, K. L. and **Carney, D. H.** Cytoplasmic microtubules affect thrombin binding and initiation of DNA synthesis. J. Supramol. Struct. and Cell. Biochem., Supplement 5:268, 1981.

13. **Carney, D. H.** Immunofluorescent visualization of thrombin binding to fibroblasts: Evidence for preclustered receptors. J. Cell Biol. 91:230a, 1981.

14. Crossin, K. L. and **Carney, D. H.** Microtubule stabilization by taxol inhibits growth factor-stimulated DNA synthesis. J. Cell Biol. 91:334a, 1981.

15. Bergmann, J. S. and **Carney, D. H.** Preclustering of thrombin receptors on mouse embryo fibroblasts analyzed by immunofluorescence; immunohistochemistry and EM autoradiography. J. Supramol. Struct. and Cell. Biochem., Supplement 6, 1982.

16. Crossin, K. L. and **Carney, D. H.** Temporal and spatial microtubule rearrangements may be required to initiate cell division. J. Supramol. Struct. and Cell. Biochem., Supplement 6, 1982.

17. Hillman, G. R. and **Carney, D. H.** Computer-assisted measurement of fluorescent ligand binding to subcellular structures. Fed. Proc.,

18. Bergmann, J. S. and **Carney, D. H.** Thrombin-receptor interaction is necessary for initiation of cell proliferation. J. Cell Biol. 95:201a, 1982.

19. Ball, R. L., Albrecht, T. B. and **Carney, D. H.** Microtubule involvement in initiation of DNA synthesis by human cytomegalovirus. J. Cell Biol. 95:3551, 1982.

20. Stiernberg, J., **Carney, D. H.** and LaBelle, E. F. Role of ion fluxes in initiation of cell division. J. Cell Biol. 95:236a, 1982.

21. Bergmann, J. S., Thomas, I. and **Carney, D. H.** Partial purification of a fibroblast growth factor from calf and horse serum which utilizes the thrombin receptor system. J. Cell Biol. 97:394a, 1983.

22. Stiernberg, J., LaBelle, E. F., Fenton, J. W., II, and **Carney, D. H.** Early stimulation of Rb^+ influx does not correlate with initiation of DNA synthesis. J. Cell Biol. 97:339a, 1983.

23. Thompson, W. C., Herbosa, G. J., Baker, J. B. and **Carney, D. H.** Monoclonal antibody visualization of thrombin, thrombin-receptors and protease-nexin. J. Cell Biol. 97:410a, 1983.

24. Bergmann, J. S. and **Carney, D. H.** Cell affinity purification of a thrombin receptor-binding growth factor. J. Cell. Biochem., Supplement 8A:248, 1984.

25. **Carney, D. H.** and Stiernberg, J. Initiation of DNA synthesis by thrombin involves two separate cell surface interactions. J. Cell. Biochem., Supplement 8A:261, 1984.

26. Herbosa, G. J., Thompson, W. C. and **Carney, D. H.** Thrombin receptor characterization by monoclonal antibodies. J. Cell. Biochem., Supplement 8A:273, 1984.

27. Thompson, W. C., Bradley, M. L. and **Carney, D. H.** Interaction of thrombin receptors with the cytoskeleton affects the rate of thrombin dissociation. J. Cell. Biochem., Supplement 8A:285, 1984.

28. Albrecht, T., Li, J. L. H., Ball, R. L., Nokta, M., Thompson, W. C. and **Carney, D. H.** Cytoskeletal related responses to human cytomegalovirus (CMV) infection. J. Cell. Biochem., Supplement 8B:187, 1984.

29. Thompson, W. C. and **Carney, D. H.** Mitogenic responsiveness of mouse embryo cell lines with high affinity alpha-thrombin receptor. J. Cell Biol. 99:417a, 1984.

30. Scott, D. L., **Carney, D. H.** and LaBelle, E. F. Thrombin stimulates phosphorylation of phosphatidyl inositol. J. Cell Biol. 99:417a, 1984.

31. Ball, R. L., Thompson, W. C., Asai, D. J., Albrecht, T. and **Carney, D. H.** Use of radiolabeled monoclonal anti-tubulin antibodies to quantitate microtubular tubulin in situ. J. Cell Biol. 99:417a, 1984.

32. Gordon, E. A, Stiernberg, J. and **Carney, D. H.** Thrombin binding to high-affinity receptors increases cAMP levels in resting fibroblasts. J. Cell Biol. 99:417a, 1984.

33. Herbosa, G., Thompson, W. C. and **Carney, D. H.** Monoclonal antibody to high-affinity thrombin receptors generates one part of the signal to initiate cell proliferation. J. Cell Biol. 99:417a, 1984.

34. Morris, D. L., Ward, J. B., Jr. and **Carney, D. H.** Thrombin promotes growth of transformed foci in Balbc/3T3 cells. J. Cell Biol. 99:417a, 1984.

35. **Carney, D. H.**, Gordon, E. A, Scott, D. L. and LaBelle, E. F. Thrombin stimulated phosphoinositide metabolism appears necessary for thrombin mitogenesis. Fed. Proc. 44:414, 1985.

36. **Carney, D. H.**, Gordon, E. A, Scott, D. L. and LaBelle, E. F. Role of phosphoinositide turnover in thrombin mitogenesis. Int. Cong. of Biochem., Amsterdam MO 406, 1985.

37. Herbosa, G. J., Sandhu, G. and **Carney, D. H.** Affinity purification and reconstitution of the high-affinity thrombin receptor using monoclonal antibodies. J. Cell Biology, 101:114a 1985.

38. **Carney, D. H.**, Herbosa, G. J. and Glenn, K. C. Thrombin peptide interacts with high-affinity thrombin receptors initiating part of the proliferative signal. J. Cell Biology, 101:114a, 1985.

39. Ball, R. L., Albrecht, T., Thompson, W. C. and **Carney, D. H.** Microtubule involvement in initiation of cellular DNA synthesis by growth factors, tumor promoters and oncogenic DNA viruses. J. Cell Biochem. 10C:110, 1986.

40. Bergmann, J. S. and **Carney, D. H.** Tissue plasminogen activator interacts with thrombin receptors and stimulates DNA synthesis in mouse embryo fibroblasts. J. Cell Biochem. 10C:111, 1986.

41. Gordon, E. A, Bergmann, J. S. and **Carney, D. H.** Tumor promoters increase binding of ^{125}I-thrombin to receptors on hamster and mouse embryo fibroblasts. J. Cell Biochem. 10C:196, 1986.

42. **Carney, D. H.** Protease activation of cellular activities: Possible roles for both receptor occupancy and enzymic activity. J. Cell Biochem. 10A:256, 1986.

43. Herbosa, G. J. and **Carney, D. H.** Tunicamycin treatment inhibits binding of ^{125}I-thrombin to high-affinity receptors on hamster fibroblasts. J. Cell Biol. 103:332a, 1986.

44. **Carney, D. H.**, Herbosa, G. J., Bergmann, J. S. and Gordon E. A. Involvement of high and low affinity thrombin receptor interactions in initiation of cell proliferation. J. Cell Biol. 103, 438a, 1986.

45. Belloni, P. N., Nicolson, G. L. and **Carney, D. H.** Differential thrombin binding and growth stimulation of various organ-derived vascular endothelial cells. J. Cell. Biochem. 11A:50, 1987.

46. Bergmann, J. S. and **Carney, D. H.** Factors IX and X interact with high-affinity thrombin receptors and stimulate cell proliferation. J. Cell Biol. 105, 191a, 1987.

47. Ball, R. L., Albrecht, T. and **Carney, D. H.** Involvement of the microtubule equilibrium in initiation of DNA synthesis by growth factors and tumor promoters. J. Cell Biol. 105, 189a, 1987.

48. Gordon, E. A and **Carney, D. H.** Role of PI turnover and activation of protein kinase C in thrombin-stimulated cell proliferation. J. Cell Biol. 105, 188a, 1987.

49. Frost, G. H. and **Carney, D. H.** HPLC purificaiton of the thrombin receptor from hamster and mouse fibroblasts. J. Cell Biol. 105, 235a, 1987.

50. Gordon, E.A, and **Carney, D.H.** Role of protein kinase C in thrombin-stimulated cell proliferation. J. Cell Biol. 107, 275a, 1988.

51. Mann, R., **Carney, D.H.**, Christi, J., Herndon, D.N., Heggers, J. and Robson, M.C. Synthetic thrombin-binding peptide increases incisional breaking strength. Society of University Surgeons and Plastic Surgery Research Council, 1988.

52. Pernia, S.D., Redin, W.R. and **Carney, D.H.** Synthetic thrombin-receptor peptide enhances healing of full thickness dermal excisions. J. Cell Biol. 109, 28a, 1989.

53. Wang, F., Thompson, W.C. and **Carney, D.H.** Use of thrombin responsive and nonresponsive cell lines to analyze second messengers involved in thrombin mitogenesis. J. Cell Biol. 109, 212a, 1989.

54. James, O.A., Thompson, W.C. and **Carney, D.H.** Microtubule involvement in thrombin receptor anchorage and affinity. J. Cell Biol. 109, 267a, 1989.

55. Scott, D.S. and **Carney, D.H.** Synthesis and use of a non-radioactively labeled human alpha-thrombin derivative in a new type of antigen capture assay: The biotinylated overlay assay. J. Cell Biol. 111, 59a, 1990.

56. Pernia, S.D., Berry, D.L., Redin, W.R. and **Carney, D.C.** A synthetic peptide representing the thrombin receptor-binding domain Eenhances wound closure in vivo. SAAS Bulletin: Biochem. & Biotech. 38, 1990.

57. Warner, W S., Redin, W.R., Paulley, V.T. and **Carney, D.H.** Effect of thrombin peptides on full dermal excisional wound closure in normal mice. Wound Healing Society, 1991.

58. Roark, L.M., Redin, W.R., Carraway, K. and **Carney, D.H.** Thrombin peptides promote wound healing in steroid treated rats. Wound Healing Society, 1991.

59. Naldini, A., **Carney, D.H.**, Bocci, V. and Klimpel, G.R. Thrombin enhances T cell activation. FASEB 5: A1378, 1991.

60. **Carney, D.H.**, Redin, W., Paulley, V., Carraway, K, & Warner, S. Effects of thrombin receptor activating peptide (TRAP) on closure of full dermal excisions in diabetic mice. J. Cell. Biochem. 15F:193a, 1991.

61. Pernia, S.D., Redin, W.R., & **Carney, D.H.** Assessment of enhanced closure of full-thickness wounds in rats treated with TRAP-508: Contraction vs reepithelization. J. Cell. Biochem 15F:198a, 1991.

62. **Carney, D.H.**, Ramakrishnan, S.R., & Scott, D.L. Relationship between high-affinity mitogenic receptors on fibroblasts and the recently cloned functional megakaryocyte thrombin receptor. J Cell Biol. 115:249a, 1991.

63. Kim. D.W. & **Carney, D.H.** Thrombin induction of c-myc and c-fos occurs through a specific subset of signals generated by thrombin-thrombin receptor interactions. J Cell Biol. 115:16a, 1991.

64. James, O.A., Thompson, W.C. & **Carney, D.H.** Relationship between cytoskeletally-anchored thrombin receptors on mouse embryo fibroblastic cells and the cloned functional thrombin receptor. Mol. Biol. of the Cell 3:331a, 1992.

65. Kim, D.W., Wang, F., & **Carney, D.H.** Induction of c-fos in thrombin-responsive cell lines by thrombin and synthetic thrombin receptor peptide. Mol. Biol. of the Cell 3:331a, 1992.

66. Ramakrishnan, S., Scott, D.L., Hensler, T., & Carney, D.H. The cloned functional thrombin receptor appears to be a component of the previously identified high-affinity thrombin receptor complex. Mol. Biol. of the Cell 3:331a, 1992.

67. Godfrey, D., Hallberg, C., Carney, D.H., Redin, W. & Trocme, S.D. Enhancement of corneal wound healing by thrombin receptor activating peptide in the rat. Invest. Opht. Vis. Sci. 34:1015, 1992.

68. Hallberg, C., Ramakrishnan, S., Carney, D.H., Brysk, M.M., and Trocme, S.D. Thrombin receptor-activating peptide promotes proliferation of cultured human corneal epithelium. Invest. Opht. Vis. Sci. 34:1011, 1992.

69. Ramakrishnan, S, & Carney, DH. 1993. Effect of thrombin and thrombin receptor peptides on neutrophil chemotaxis. Mol. Biol. Cell 4: 1993.

70. Carney, D.H., Hallberg, C.K., Redin, W., Trocme, S.D. Autoradiographic evidence of thrombin receptor activating peptide-508 induced corneal epithelial cell proliferation during wound healing. Invest. Opht. Vis. Sci. 35: 1993.

71. Soares, L. E., Carney, D.H., Froelich,C., and Klimpel, GR. Alpha thrombin induces IL-6 production by human lung fibroblasts. FASEB, 1993.

72. Dickey, W.D., Valentich, J.D., Powell, D.W., Carney, D.H., Stiernberg, J. Effect of α-thrombin and thrombin receptor peptides on intestinal subepithelial myofibroblast morphological differentiation. Gastro (Abst.) 1995.

73. Soares, L. E., Carney, D.H. and Klimpel, GR. Characterization of thrombin enhancement of T cell activation. FASEB, Cooper Mountain, Colorado, August, 1995.

74. Naldini, A., Sower, L., Carrara, F., Pessina, G.P., and Carney, D.H., Thrombin enhances the release of IL-6 by human monocytes through a differentiation-linked mechanism. FASEB Journal 11:A453, 1997.

75. Taylor, B.E. and Carney D.H., Human vascular endothelial cells from large and small vessels differ in growth responses to thrombin. FASEB Journal 11:A453, 1997.

76. Sower, L.D., Payne, D.A., Meyers, B.K. and Carney, D.H. Thrombin peptide TRAP-508 induces differential gene expression in fibroblasts. Presented at the American Society of Cell Biology, Washington, D.C., Molecular Biology of the Cell 8:243a, 1997.

77. Stiernberg, J., Redin, W.R., Warner, S, and Carney, D.H. Thrombin peptide, TP508 stimulates wound healing through a non-proteolytic mechanism. Wound Repair and Regeneration. 6:(3) A265, 1998.

78. Stiernberg, J., Redin, W.R., Warner, S, and Carney, D.H. Cellular antimicrobial action in wounds is stimulated by the thrombin peptide TP508. Wound Repair and Regeneration. 6:(3) A265, 1998.

79. Carney, DH., Carney, DS, Meyer, R. Sower, LE. and Crowther, R. Evidence for multiple thrombin receptors on fibroblasts: Binding of thrombin and PAR1 receptor ligand (SFLRRY) reveal differences in numbers of binding sites per cell. Presented at

the American Society of Cell Biology, SanFrancisco, CA Dec. 1998, Molecular Biology of the Cell 9: 237a, 1998.

80. Stiernberg, J., Sower, L.E., Gerdes. L., Ramakrishnan, S, Redin, W.R., and **Carney, D.H.**. Cellular antimicrobial action in wounds is stimulated by the thrombin peptide, TP508. Presented at the American Society of Cell Biology, SanFrancisco, CA Dec. 1998, Molecular Biology of the Cell 9: 237a, 1998.

81. Sower, L.E. and **Carney, D.H.**. Thrombin peptide, TP508, enhances proliferation of peripheral blood mononuclear cells (PBMC) and T cells via a non-proteolytically activated receptor pathway. Presented at the American Society of Cell Biology, San Francisco, CA Dec. 1998, Molecular Biology of the Cell 9: 236a. 1998.

82. Crowther, R.S., Simmons, D.J., Yang, J. , Yang, S., Bi, L.X., Buford, W. L. and **Carney, D.H.** Thrombin peptide TP508 significantly accelerates repair of fresh fractures. Texas Mineralized Tissue society, Austin TX, August 1998.

83. Simmons, D.J., Yang, J. , Yang, S., Bi, L.X., Buford, W. L. Crowther, R.S., and **Carney, D.H.** Thrombin peptide significantly accelerates repair of fresh fractures. Comparative Endocrinology of Calcium Regulation ASBMR-International Bone Mineralization Society, SanFrancisco, CA, November 1998.

84. Simmons, D.J., Yang, J. , Yang, S., Bi, L.X., Buford, W. L. Crowther, R.S., and **Carney, D.H.** Thrombin peptide accelerates repair of fresh fractures. 45th Annual Meeting, Orthopaedic Research Society, Anaheim, CA, February, 1999.

85. Sower, L.E. and **Carney, D.H.** Thrombin peptide, TP508, inhibits collagenase synthesis stimulated by TNFα and proteolytically active thrombin. FASEB, 1999.

86. Fritz, P.H. and **Carney, D.H.** Cell Activation by thombin Peptide TP508 Stimulates a pattern of Gene Expression Distinct from that induced by thrombin or SFLLRNP. Molecular Biology of the Cell, 10: Supplement (November 1999).

87. Sower, L.E., Huang, Y., Norfleet, A.M., **Carney, D.H.** Thrombin peptide TP508 induces proliferation and migration of keratinocytes. Molecular Biology of the Cell, 10: Supplement (November 1999).

88. Norfleet, A.M., Redin, W.R., Sower, L.E., Stiernberg, J., **Carney, D.H.** Accelerated recruitment of inflammatory cells to dermal wounds by the thrombin peptide, TP508. Molecular Biology of the Cell, 10: Supplement (November 1999).

89. Bergmann, J.S., Meyers, B., **Carney, D.H.** Effect of thrombin peptide, TP508, on proliferation and migration of human endothelial cells. Molecular Biology of the Cell, 10: Supplement (November 1999).

90. Ryaby, JT, Campbell, MB, **Carney, DH**, Crowther, RS., Yang, J, Simmons, DJ, Zoltan, JD, and Magee, FP, Acceleration of fresh fracture healing with an injectable thrombin peptide in a rat model. Am. Academy of Orthopaedic Surgeons, 2000.

91. Bergmann, J.S., Keherly, MJ., **Carney, DH.** CDNA expression array analysis identifies early changes in fibroblast gene expression induced by thrombin peptide TP508. Molecular Biology of the Cell, 11:456-457a. Supplement (November 2000).

92. Norfleet, AM., Redin, WR., Morshedi, PJ., and **Carney, DH**. Thrombin peptide TP508 accelerates dermal wound healing with an immediate, delayed, or double treatment regimen: role of leukocytes. Molecular Biology of the Cell, 11:464a. Supplement (November 2000).

93. Coleman, CL, Wortham, AM, Norfleet, AM, Yang, J, Sriram, V, Medford, DJ, Stouffer, GA, Waxman, S, and **Carney, DH**. Systemic injection of thrombin peptide TP508 mitigates angioplasty-related restenosis in hypercholerterolemic rabbit illiac arteries. FASEB Supplement Experimental Biology LB14 (April 2001).

94. Ryaby, JT, **Carney, DH**, Crowther, RA, Yang, J, and Grande, DA. Repair of osteochondral defects in the rabbit with a novel, thrombin-related peptide. International Tissue Repair, Frieberg Germany. (November 2001)

95. Naldini, A, **Carney, DH**, Pucci, A, and Carraro F. Thrombin peptide TP508 (Chrysalin®) upregulates cytokines IL-2, IL-6, and IL-12 in pre-activated peripheral blood mononuclear cells. Molecular Biology of the Cell, 12: 256a. Supplement (November 2001).

96. Moller, ML, Keherly, MJ, and **Carney, DH**. The thrombin peptide TP508 is a potent chemotactic agent for human neutrophils (PMNs). Molecular Biology of the Cell, 12: 257a. Supplement (November 2001).

97. Bergmann, JS, Laird, AC, and **Carney, DH**. Thrombin and thrombin peptide TP508 (Chrysalin®) bind to a high affinity thrombin receptor that appears to be larger than known members of the proteolytically activated receptor (PAR) family. Molecular Biology of the Cell, 12: 330a. Supplement (November 2001).

98. Saeed, M, Keherly, MJ, Nguyen, Y, Bergmann, JS, Whitson, BS, and **Carney DH**. Yeast Two-Hybrid Analysis to identify receptor proteins that interact with thrombin or the thrombin peptide TP508. Molecular Biology of the Cell, 12: 330a. Supplement (November 2001).

99. Grande, D., Karnaugh, R., Ryaby, J, Dines, D., Razzano, P, Crowther, R., **Carney, D**, and Wu,D. "In vivo evaluation of the synthetic thrombin peptide, TP508, in articular cartilage repair" Orthopaedic Research Society Meeting, February 2002 (Cartilage Repair Poster 447).

100..Boyan, B, Lopez, D., **Carney, D**, Ryab, J, Sylvia, V, Dean, D, and Crowther, R. Thrombin peptide (TP508) differentially regulates phenotypic expression of costachondral chondrocytes enhancing cartilage matrix synthesis but not endochondral maturation. Orthopaedic Research Society Meeting, February 2002 (Tissue Engineering, Poster 465).

101. Ryaby, J, DiJorio, S, Crowther, R, Breunig, T, Kinneym J, Yang, J, and **Carney, D**. Repair of segmental defects in the rabbit with the thrombin-related peptide, TP508. Orthopaedic Research Society Meeting, February 2002 (Bone Grafts/Substitutes, Poster 735).

102. Ryaby, J., **Carney, D**, Crowther, R, Yang, J, and Grande, D. Repair of osteochondral defects in the rabbit, with a novel, thrombin related peptide (TP508). American Academy of Orthopaedic Surgeons, February 2002 (Basic Science, Poster 168).

MANUSCRIPTS "In Press":

Naldini, A., Pucci, A., Carney, DH., Fanetti, G., and Carranro, F. Thrombin enhancement of Interleukin-1 expression in mononuclear cells through proteinase-activated receptor-1. Cytokine In Press.

Fossum, T.W., Anderson, D.W., Coleman, C.L., Carney, D.H., Healing the heart: New options for repair of ischemic and infracted myocardium. Turkish Journal of Cardiology, In Press.

MANUSCRIPTS "SUBMITTED":

MANUSCRIPTS IN PREPARATION:

Naldini, A., Carraro, F. T. Balderi, **Carney, DH.** Thrombin Peptide TP508 stimulates cytokine expression and phosphorylation of mitogen-activated protein kinases in human mononuclear cells.

Sheller, M.R., Crowther, R. S., Yang, J., Kinney, J.H., DiJorio, S., Breuig, T., Ryaby, J.T., **Carney, D.H.** Repair of rabbit segmental defects with thrombin peptide TP508.

Grande, D., Karnaugh, R., Ryaby, J, Dines, D., Razzano, P, Crowther, R., Wu, D. and **Carney, D.H.** Stimulation of articular cartilage repair in rabbit osteochondral defects by thrombin peptide TP508.

Warner, W.S., Hoakanson, J.A., **Carney, D.H.** Mathematical modeling using Gomperts life table analysis to predict efficacy of TP508 in accelerating closure of full-thickness dermal excisional normal mouse wounds.

Norfleet, A., Siemberg, J., Warner, W.S., Redin, W.R., and **Carney, DH.** Thrombin peptide TP508 accelerates healing of excisional wounds in genetically diabetic Db/Db mice and streptozotocin induced diabetic mice.

Taylor, B.E. and **Carney, D.H.** Thrombin and thrombin peptide, TP508, in combination have divergent growth effects on large and small vessel vascular endothelial cells.